Design and Synthesis of Heterocyclic Compounds for Sensing and Bioimaging

Synopsis

Submitted

In

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Introduction:

Organic fluorophores operating in the optical window of biological tissues, namely in the deep-red and near-infrared (NIR) region of the electromagnetic spectrum, offer several advantages for fluorescence bioimaging applications owing to the appealing features of long-wavelength light, such as deep tissue penetration, lack of toxicity, low scattering, and reduced interference with cellular autofluorescence.[1]

Substitution can be employed to proficiently tune the photophysical properties of chemosensors. The effect of substituents on the absorption and emission properties of fluorescent probes was investigated. In this direction salicylaldehyde (S), N-diethylamino-salicylaldehyde (D), and nitro-salicylaldehyde (W)-based quinoline Schiff base derivatives were investigated with hydrazine and studied for their photophysical properties.[2] Recently, a series of fluorescent probes have been designed and reported for detecting hydrazine that employ various reaction-based sites such as 4-bromobutyric acid, levulinate, benzothiazole acetonitrile, o-phthaldehyde, β-diketone, and acetyl. [3] Heterocyclic derivatives can chelate with metal ions, leading to changes in their optical, electrochemical, or fluorescent properties. This ability makes them useful in detecting metal ions in environmental samples, biological fluids, and industrial processes.

Heterocyclic compounds are pivotal in sensing and imaging applications due to their diverse chemical structures and properties. Their unique characteristics, such as fluorescence, photoactivity, and electron transfer abilities, make them invaluable in various sensing techniques, including fluorescence sensing, electrochemical sensing, and colorimetric sensing.

Moreover, their tunable properties allow for the design of sensors with high selectivity and sensitivity towards specific analytes, making them indispensable in environmental monitoring, medical diagnostics, and drug discovery. In imaging, heterocyclic compounds serve as versatile contrast agents and fluorescent probes for visualizing biological processes, detecting diseases, and monitoring therapeutic interventions. Their ability to target specific cellular structures and biomolecules while providing excellent signal-to-noise ratios makes them indispensable tools in modern biomedical imaging modalities such as fluorescence microscopy, magnetic resonance imaging (MRI), and positron emission tomography (PET). Overall, heterocyclic compounds play a vital role in advancing sensing and imaging technologies, driving innovation in various scientific and medical fields.{4,5}Heterocyclic derivatives have been employed in environmental sensing platforms for detecting pollutants like aromatic hydrocarbons, pesticides, and heavy metals. Their ability to undergo selective chemical reactions with these pollutants enables the development of sensors for environmental monitoring applications. These derivatives can also act as pH indicators due to their pH-dependent fluorescence or color changes. This property can be utilized in developing optical pH sensors for monitoring pH changes in biological and environmental samples.

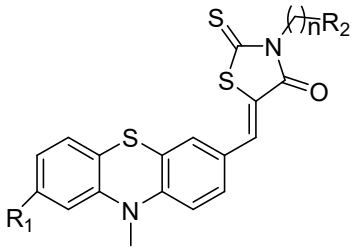


Fig. 1

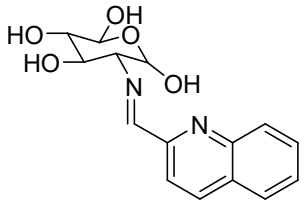


Fig. 2.

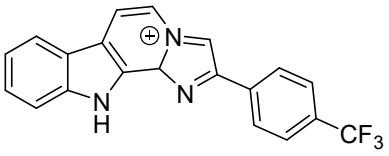


Fig. 3

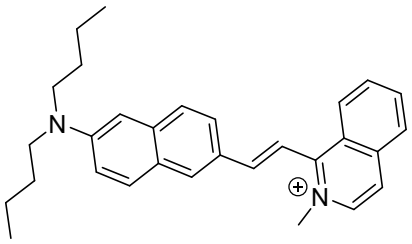


Fig. 4

The theranostic chemical space was enriched using scaffolds such as phenothiazine, cyanine, quinoline, curcumin and curcumin surrogates, styryl benzenes, and coumarin and coumarin analogues, with some examples having great potential. The phenothiazine was selected as the backbone scaffold, adding rhodanine units to establish the overall theranostic structure[6]. Shengju et. Al., reported a selective and sensitive fluorescent sensor for the detection of Hg^{2+} in natural water by incorporating the recognized fluorophore quinoline group and a water-soluble D-glucosamine group within one molecule (Fig.2).[7]

β-carboline-based novel chemosensor, containing an acidic proton attached to indole nitrogen was reported by Das et.al.,(Fig.3). Fluoride (F^-) uptook that acidic proton from the sensor and changes the colour of the sensor solution from colourless to yellow and a new green fluorescence band originates around 554 nm. It was found to be selective towards F^-, as incubation of other anions hardly imposes any visual color change or fluorescence property.[8] Wong et al. formulated fluorescent probes based

upon carbazole replacement with the 2-naphthylamine framework, as well as quinolinium N-tail modifications and quinoline replacement with isoquinoline, searching for the optimal theranostic properties.[9, 10]

In the last few years, several examples of theranostics have been developed to combine and therapeutic outcomes, aiming to change the current status of research and drug discovery. The integration of imaging and therapeutic tools in one single chemical entity has the potential to move clinical practice toward personalized medicine. In the past decade, the theranostic chemical space was enriched using scaffolds such as phenothiazine, cyanine, quinoline, curcumin and curcumin surrogates, styrylbenzenes, and coumarin and coumarin analogues, with some examples having great potential.

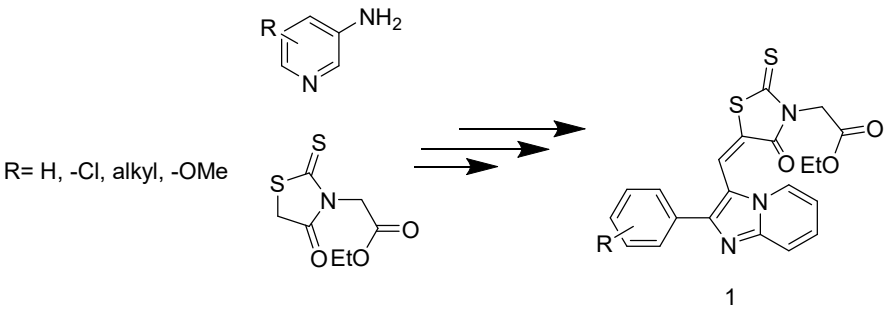
The design strategies are not well established, lacking critical insights into the geometry of the architectural scaffold and the binding pocket of the target macromolecules. This comprehensive analysis will encourage current research work to develop imaging probes together with therapeutic tools to provide effective diagnosis, paving the way to personalized medicine. The successful development of optical theranostics that can assist early-stage monitoring and serve as complementary tools in drug discovery can change the paradigm forever.

1.2 Methodology of the study in brief:

1.2.1. Synthesis of Heterocyclic scaffold: Synthesis of heterocyclic scaffold will be done as represented in scheme 1 and 2.

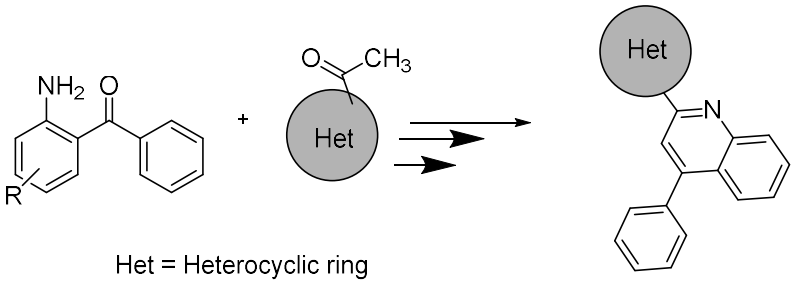
Scheme 1:

In this scheme, we propose to synthesize final product by utilizing imidazopyridine and 2-thiooxothiazolidine-4-one moiety.



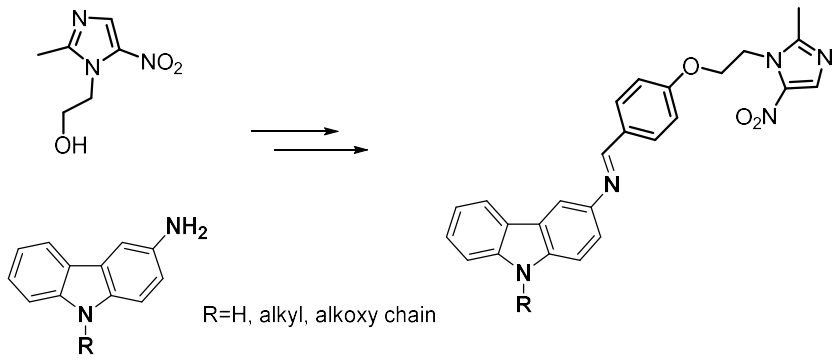
Scheme 2:

In this scheme, we propose to synthesize quinoline derivatives using Friedlander sunthesis:

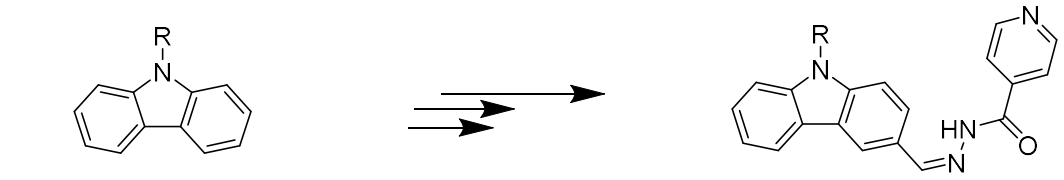


Scheme 3:

In this scheme, we propose to synthesize final product by following method:

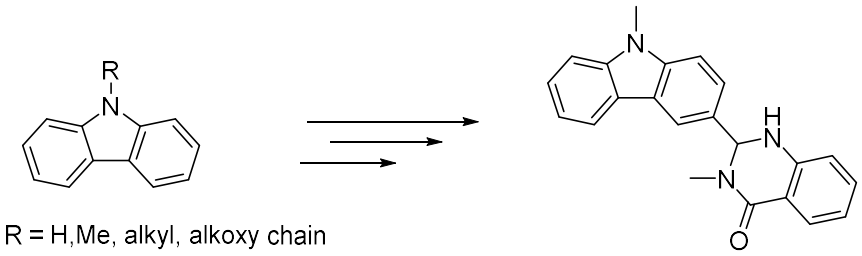


Scheme 4: In this scheme, we propose to synthesize final product by following method:



R = H, Me, alkyl, alkoxy chain

Scheme 5: In this scheme, we propose to synthesize final product by following method:



R = H,Me, alkyl, alkoxy chain

If there is a need for further modifications, they can be carried out accordingly to meet the requirements of the research.

Characterization of Compounds: NMR, Mass, HRMS, UV and IR can be carried out at IIT Patna, BHU Varanasi or CSIR-CDRI.

1.2.2. Photophysical analysis: Photophysical properties of synthesized compounds will be studied using UV-Visible and Fluorescence spectroscopy at IIT Patna, BHU Varanasi or CSIR-CDRI.

1.2.3. Biological activities : Antialzheimer's, anticancerous, antimicrobial activities can be studied in collaboration at CSIR-CDRI, BHU Varanasi or NIPER institutes.

1.3. References:

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Signature of the Candidate

The candidate has agreed to complete the research work under my supervision within the time limit.

Signature of the Supervisor/Designation/

Department/College/University